REMARKS/ARGUMENTS

Claims 1-28 are pending. Claims 1 and 16 have been amended to recite "wherein" instead of "each adapted for release such that."

I. Objection to the specification

The Examiner contends that the Applicant failed to remove the hyperlink from the specification at page 32, line 32. Applicant did make this amendment in the response filed July 26, 2006. In so doing, Applicant deleted the internet address hyperlink by cross-out and added the internet address without the hyperlink. Additions to the specification must be shown by underlining the added text. 37 C.F.R. §1.121(b)(ii). It is this underline that was mistaken for a hyperlink by the Examiner, i.e., Applicant merely added the address back into the specification without the hyperlink.

II. The first rejection under 35 U.S.C. § 112, second paragraph

Claims 1-28 have been rejected under 35 U.S.C. § 112, second paragraph because the Examiner contends that the claims omit elements that are essential to obtain the claimed release profile.

The Examiner alleges that the recitation of a release profile alone does not impart any physical or material property to the composition and "[a]s a result, the claims do not distinguish over a pharmaceutical combination simply comprising amphetamine in base and/or salt form" (Office Action, page 4). Applicant respectfully traverses this rejection.

Applicant's understanding is that a rejection omitting an essential element is typically made under the first paragraph of section 112 (for non-enablement), and a section 112, second paragraph rejection typically relates to an alleged failure to interrelate essential elements of the invention. See MPEP 2172.01. In any case, the instant claims do not omit an essential element or fail to interrelate these elements. An essential element is an element "described by the applicant(s) as necessary to practice the invention." MPEP 2173.02. Here, all essential elements *are* claimed, i.e., l- and d- amphetamine, each in base and/or salt form, and an l- to d- amphetamine release ratio that increases during the day.

As the Examiner acknowledges, the instant specification discloses a variety of ways the claimed pharmaceutical combinations can be obtained. See, Office Action, page 4. For example, the specification discloses that:

> without limiting the invention in any way, modes include administering more of the d-isomer early in the day (e.g., about 6:00 am to about 11:00 am), e.g., only d-isomer or a molar ratio of d/l of about 1.5 to about 5/1, or higher or lower, (e.g., 3/1 as in Adderall®), and then administering a higher ratio of the l-isomer later in the day (e.g., about 12:00 noon or later, e.g., 4:00 pm, 6:00 pm, etc.), e.g., only l-isomer, or a molar ratio of l/d of about 1.5 to about 5/1, or higher or lower. It is also possible to administer more l-amphetamine than d-amphetamine earlier in the day or the same amounts of each (e.g., in racemic form), as long as the increased l-ratio later in the day of this invention is achieved. Similarly, the doses of each isomer can be administered in the most varied of ways, e.g., each can be administered separately, together in a single formulation, concurrently, sequentially, etc.

(Specification, page 5)

"In determining whether an unclaimed feature is critical, the entire disclosure must be considered. Features which are merely preferred are not to be considered critical." MPEP 2164.08(c). None of the disclosed but unclaimed features (e.g., an immediate release dosage form or a single dosage form) is described as necessary. These features are embodiments of the invention, which contribute to the enabling disclosure, but should not be considered critical or essential.

Different amphetamine pharmaceutical compositions are well known in the art, e.g., d-isomer alone, racemic mixtures. One of ordinary skill in the art, without undue experimentation, could combine these different dosage forms in many different ways, either in one dosage form or separate dosage forms, to obtain the claimed release ratio profile. Accordingly, this rejection should be withdrawn.

III. The second rejection under 35 U.S.C. § 112, second paragraph

Claims 1 and 16 have been rejected under 35 U.S.C. § 112, second paragraph because the Examiner contends that the limitation "each adapted for release" is not "an active requirement of

the pharmaceutical combination and reads upon a future 'adaptation' of the l- and d- amphetamines" (Office Action, page 4).

Amended claims 1 and 16 do not recite "each adapted for release." Accordingly, this rejection should be withdrawn.

III. The prior art rejections

A. The rejections under 35 U.S.C. § 102(b)

Claims 1-11, 14-15 and 22-24 have been rejected as anticipated by U.S. Patent No. 6,322,819. The '819 patent anticipates, according to the Examiner, because "[r]ecitations of function, or in the present case, release, of the claimed composition, in the absence of a physical or structural difference, do not patentably limit the composition" (Office Action, page 6). Thus, the instant claims "solely" require the presence of both l- and d- amphetamine, in base and/or salt form, in an effective amount. *Id.*

Claims 1-16 and 27-28 have been rejected as anticipated by Patrick et al., "Pharmacology of Methylphenidate, Amphetamine Enantiomers and Pemoline in Attention-Deficit Hyperactivity Disorder," 1997, pp. 527-546. Patrick discloses ADDERALL®.

The Examiner alleges that "the recitation of the release profile of the combination is a resultant function or intended use of the composition and is not a patentable distinction over the prior art" (Office Action, page 5).

Respectfully, a release profile is not a function or use, as the Examiner contends, but a physical characteristic of the claimed pharmaceutical combination. Further, even if the release ratio profile is labeled a functional limitation (it is not), the MPEP clearly states that functional limitations cannot be ignored: "A functional limitation must be evaluated and considered, just like any other limitation of the claim ..." MPEP 2173.05(g); see also *Hofer v. Microsoft Corp.,* 74 USPQ2d 1481 (Fed. Cir. 2005) (cited in MPEP 2173(g)) ("[A] 'whereby' clause generally states the result of the patented process. However, when the 'whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention.").

Accordingly, when the entirety of the instant claims is considered, the cited references are not anticipatory because they do not disclose the claimed release ratio profile.

B. The rejections under 35 U.S.C. § 103(a)

Claims 1-28 have been rejected as obvious over Patrick in view of WO 2002/039998 (Epstein), the '819 patent, STN Registry No. 156-34-3, and Tulloch et al., Pharmacotherapy, 2002;22(11):1405-1415.

The Examiner acknowledges that Patrick does not teach: (1) the claimed total dose of amphetamine per day; (2) the administration of l- and d- amphetamine in a single, staged-release, immediate release, pulse released and/or sustained or controlled release dosage form; and (3) the administration of amphetamine in two doses, the first having an l/d isomer ratio of 1:3 or only d-isomer and the second dose having an l/d isomer ratio of greater than about 1:1 or only l-isomer (Office Action, pages 9-10). The Examiner contends, however, that the differences between Patrick and the instant claims would have been obvious to one of ordinary skill in the art.

According to the Examiner, determination of the optimum dosage regimen to treat ADHD is routine in the art, and the '819 patent discloses the claimed dosage forms. Further, the Examiner contends that Epstein discloses that l-amphetamine has fewer addictive properties and greater memory enhancing effects compared to d-amphetamine, and Tulloch discloses that the d/l ratio in ADDERALL® is 3:1. The Examiner concludes that in light of these disclosures, it would have been obvious to one of ordinary skill in the art to modify the composition disclosed in Patrick to include more l- than d- isomer.

Further, the Examiner alleges that it would have been obvious to use both the d- and l-isomer because "it flows logically ... that each was known to be administered for the same therapeutic endpoint and it is generally obvious to use in combination two or more agents that have previously been used separately for the same purpose" (Office Action, pages 12-13).

Even if Applicant agreed with the Examiner's assertions (we do not), a *prima facie* case of obviousness has not been put forth. Accepting for the sake of argument that the prior art suggests using more l- than d- amphetamine, one does not arrive at the instantly claimed invention. None of the cited prior art, whether alone or in combination, discloses or suggests increasing the release ratio

of l- to d- amphetamine as the day progresses. Further, the prior art does not provide the motivation to one of ordinary skill in the art to vary the l- to d- release ratio as the day progresses in the claimed manner.

For the reasons stated above, this rejection should be withdrawn.

IV. Provisional obviousness-type double patenting rejections

Claims 1-15 and 22-26 have been provisionally rejected for obviousness-type double patenting over the composition claims of U.S. Patent Nos. 6,605,300; 6,322,819 or 6,913,768 and U.S. Patent Application Nos. 11/091,011; 10/758,151; 11/030,174 or 11/150,311. Claims 16-21 have been provisionally rejected for obviousness-type double patenting over the method claims of U.S. Patent No. 6,913,768 and U.S. Patent Application Nos. 11/030,174 or 11/150,311.

Applicant requests that these provisional rejections be held in abeyance until allowable subject matter has been identified.

Conclusion

No new matter has been added by these amendments. In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

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Respectfully submitted,

By _____

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